

WHAT IS CLAIMED IS:

1. A method for producing a therapeutic
radioconjugate of a targeting moiety bound, directly or
indirectly, to at least one relatively short lived α -
particle emitting radioisotope, said targeting moiety
being effective to deliver said radioconjugate to a
pathological site *in vivo*, said pathological site
comprising a target moiety, said targeting moiety and
said target moiety constituting a specific binding pair,
said method comprising loading onto a binding medium a
relatively long lived radioisotope, the decay sequence
of said relatively long lived radioisotope yielding
daughter isotopes that emit predominantly α - and/or β -
particles, eluting said α -particle emitting radioisotope
from said binding medium and coupling said α -particle
emitting radioisotope, substantially free of said
relatively long lived radioisotope, to said targeting
moiety.

2. A method as claimed in claim 1, wherein
said relatively long lived isotope is ^{225}Ac and said
relatively short lived α -particle emitting radioisotope
is ^{213}Bi .

3. A method as claimed in claim 1, wherein
said targeting moiety is a ligand or a ligand fragment
which binds specifically to a target moiety comprising
a cell-associated ligand binding site.

4. A method as claimed in claim 3, wherein
said targeting moiety is a ligand and said ligand
binding site comprises a cell-surface receptor.

5. A method as claimed in claim 4, wherein
said ligand is a peptide.

6. A method as claimed in claim 1, wherein said targeting moiety is an antibody or antibody fragment which binds specifically to a target moiety comprising a cell-associated antigen.

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7. A method as claimed in claim 6, wherein said targeting moiety is a monoclonal antibody and said target moiety comprises a tumor-associated antigen.

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8. A method as claimed in claim 1, wherein a plurality of said α -particle emitting radioisotopes is bound to a carrier and said carrier is coupled to said targeting moiety.

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9. A method as claimed in claim 8, wherein said carrier is human serum albumin.

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10. A method as claimed in claim 1, wherein said targeting moiety is bound indirectly to said α -particle emitting radioisotope by coupling said α -particle emitting radioisotope to a localizing moiety having binding specificity for said targeting moiety and binding said localizing moiety to said targeting moiety.

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11. A therapeutic radioconjugate produced by the method of claim 1.

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12. A therapeutic radioconjugate produced by the method of claim 2.

13. A therapeutic radioconjugate produced by the method of claim 3.

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14. A therapeutic radioconjugate produced by the method of claim 5.

15. A pharmaceutical composition comprising the therapeutic radioconjugate of claim 11 and a pharmaceutically acceptable carrier medium.

5 16. A pharmaceutical composition as claimed in claim 15 further comprising at least one scavaging agent.

10 17. A therapeutic radioconjugate comprising an α -particle emitting radioisotope, substantially without harmful gamma radiation, bound directly or indirectly to a targeting moiety, said targeting moiety being selected from the group consisting of antibody having binding specificity for tumor associated antigen,
15 an antigen binding fragment of antibody having binding specificity for a tumor associated antigen, a ligand having binding specificity for a cell surface receptor present on a tumor cell or a ligand fragment having binding specificity for a cell surface receptor present
20 on a tumor cell.

25 18. A therapeutic radioconjugate as claimed in claim 17, wherein said α -particle emitting radioisotope is ^{213}Bi .

30 19. A therapeutic radioconjugate as claimed in claim 17, wherein said targeting moiety is a ligand having binding specificity for a cell surface receptor present on a tumor cell.

35 20. A therapeutic radioconjugate as claimed in claim 19, wherein said ligand is a peptide.

40 21. A pharmaceutical composition comprising a therapeutic radioconjugate as claimed in claim 17 and a pharmaceutically acceptable carrier medium.

22. A pharmaceutical composition as claimed in claim 21, further including at least one scavaging agent.

5 23. A method for producing a therapeutic radioconjugate of a targeting moiety and ^{213}Bi , said targeting moiety being effective to deliver said radioconjugate to a pre-determined cell type, said method comprising loading ^{225}Ac on a binding medium from
10 which said ^{213}Bi is elutable, eluting said ^{213}Bi from said binding medium and coupling said ^{213}Bi , substantially free of said ^{225}Ac , to said targeting moiety, said targeting moiety being selected from the group
15 consisting of a ligand having binding specificity for a receptor associated with said pre-determined cell type or a ligand fragment having binding specificity for a receptor associated with said pre-determined cell type.

20 24. A method as claimed in claim 23, wherein said ligand is a peptide which binds specifically to a cell-surface receptor present on said pre-determined cell type.

25 25. A radioimmunoconjugate produced by the method of claim 23.

30 26. A method for killing target cells in a mammal by α -particle radiotherapy, wherein said target cells are in micrometastases having a diameter of about 1 mm or less or are in cellular diseases, said method comprising providing a sufficient quantity of ^{225}Ac to produce a therapeutically effective amount of ^{213}Bi through radioactive decay, binding the ^{225}Ac onto a substrate for immobilizing ^{225}Ac , eluting from the
35 substrate ^{213}Bi produced by bound ^{225}Ac , coupling the eluted ^{213}Bi , substantially free of ^{225}Ac , to a targeting

moiety to form a conjugate, said targeting moiety being selected from the group consisting of a ligand having binding specificity for a receptor associated with said target cell or a ligand fragment having binding
5 specificity for a receptor associated with said target cells, and administering said conjugate to said mammal to effectuate specific binding of said conjugate to said target cells.

10 27. The method as claimed in claim 26, wherein the conjugate is administered intermittently in fractions of the total amount of conjugate required to provide an effective amount of ^{213}Bi for killing said target cells in the mammal, and wherein a sufficient
15 number of fractions of sufficient quantities of conjugate are administered to kill essentially all target cells bound by said conjugate, the total quantity of α radiation administered to the mammal being less than the total quantity necessary to kill essentially
20 all target cells by administering a single dose of said conjugate.

28. The method as claimed in claim 26, wherein said conjugate is administered continuously for
25 a time sufficient to administer an effective amount of ^{213}Bi for killing said target cells in the mammal, and wherein a sufficient duration of continuous administration is maintained to kill essentially all target cells bound by said conjugate.

30 29. The method as claimed in claim 26, wherein said ligand is a peptide.

35 30. A method for detecting a pathological site in a mammal, said pathological site comprising a target moiety, said method comprising providing a

radioconjugate of a targeting moiety bound, directly or indirectly, to an α -particle emitting radioisotope, said target moiety and said targeting moiety constituting a specific binding pair, administering said conjugate to said mammal to effectuate specific binding of said conjugate to said target moiety and detecting α -particles emitted by said bound conjugate.

31. A method as claimed in claim 30, wherein said pathological site comprises diseased cells.

32. A method as claimed in claim 31, wherein said α -particle emitting radioisotope is ^{213}Bi .

33. A method as claimed in claim 32, wherein said targeting moiety is a ligand having binding specificity for a cell surface receptor present on said diseased cells.

34. A method as claimed in claim 33, wherein said ligand is a peptide.

35. A method as claimed in claim 30, wherein said pathological site is an extracellular structure.

36. A method as claimed in claim 35, wherein said α -particle emitting radioisotope is ^{213}Bi .

37. A method as claimed in claim 36, wherein said targeting moiety is a ligand having binding specificity for a receptor present on said extracellular structure.

38. A method as claimed in claim 37, wherein said ligand is a peptide.

39. A method for providing site directed
radiotherapy to a pathological site in a mammal in need
of such therapy, said pathological site comprising a
target moiety, said method comprising providing a
5 radioconjugate of a targeting moiety bound, directly or
indirectly, to an α -particle emitting radioisotope, said
target moiety and said targeting moiety constituting a
specific binding pair, and administering to said mammal
a sufficient amount of said conjugate to produce a
10 radiotherapeutic effect at said pathological site.

40. A method as claimed in claim 39, wherein
said pathological site comprises diseased cells.

41. A method as claimed in claim 40, wherein
15 said α -particle emitting radioisotope is ^{213}Bi .

42. A method as claimed in claim 41, wherein
said targeting moiety is a ligand having binding
20 specificity for a cell surface receptor present on said
diseased cells.

43. A method as claimed in claim 42, wherein
said ligand is a peptide.